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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,834	09/08/2003	Rene Gantier	119365-00005 / 922	7681
77202	7590	11/13/2008	EXAMINER	
Bell, Boyd & Lloyd LLP 3580 Carmel Mountain Road Suite 200 San Diego, CA 92130			STOICA, ELLY GERALD	
		ART UNIT		PAPER NUMBER
		1647		
		MAIL DATE	DELIVERY MODE	
		11/13/2008	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/658,834	GANTIER ET AL.	
	Examiner	Art Unit	
	ELLY-GERALD STOICA	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 22 August 2008.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1,5-8,21-23,40,46,279,307,341,343,345 and 347-356 is/are pending in the application.
- 4a) Of the above claim(s) 8 and 46 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1,5-7,21-23,40,279,307,341,343,345 and 347-356 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>06/26/2008</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

Status of the claims

1. Applicant amended the claims in the amendment of 08/22/2008. Claims 1, 5-8, 21, 23, 46, 279, 307, 341,345 and 347, were amended. Claims 9, 16- 19, 43, 44, 47-74, 139-144, 306, 308, 315,316, 332-340, 342, 344 and 346 were cancelled. The new claims 348-356 were added. Thus claims 1, 5-8, 21-23, 40, 46, 279, 307, 341, 343, 345, and 347-356 are pending. Claims 8 and 46 are withdrawn. Claims 1, 5-7, 21-23, 40, 279, 307, 341, 343, 345 and 347-356 are currently examined. The Examiner is interpreting the election of species as election of the SEQ ID 87 because in the requirement for the election/restriction Applicant was requested to choose **one** position for mutations in the IFN sequences and E41Q was chosen.

Claim objections

2. Claim 23 is objected to for containing non-elected subject matter. Since the species election lead to the election of specie SEQ ID NO 87, the other SEQ ID NOs in the claim are not elected. Appropriate correction is required.

Claim rejections necessitated by amendment

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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4. Claims 1, 21, 40, 279, 341, 343, 347, 348 and 350 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, absent a SEQ ID NO for the interferon claimed in the independent claim1, a person of ordinary skill in the art would not know which interferon alpha molecule to use for the definition of the metes and bounds of the claims. It is submitted that a specific amino acid sequence identified by a SEQ ID NO it is essential as a point of reference for the particular numbering of the amino acid sequence claimed

On page 24 of the Remarks of 06/26/2008 Applicant argues a skilled artisan would understand what is meant by the term "alpha interferon." by providing a long list of patents that include alpha Interferon. The arguments were carefully considered but not found persuasive because, absent a SEQ ID NO for the alpha interferon, one would not know where the mutation is. The numbering is not inherent to a genus of proteins as can be easily noted from cursory search for "interferon alpha" (see attached search note from NCBI).

Claim 279 is indefinite because the meets and bound of "an interferon alpha structural homolog" cannot be assessed.

On pages 44-45 of the Remarks Applicant argues the specification is detailed enough for understanding of the recitation "structural homolog". The arguments were carefully considered but not found persuasive because as presented in the arguments (and absent a particular SEQ ID NO which may be identified structurally and functionally with a specific molecule) it may be construed that the mere three dimensional structure

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of the compound claimed (structure which may be attained with a variety of amino acids residues) might not achieved the functionality of an interferon. Again, the lack of specificity of the mutations as defined in the context of a SEQ ID NO renders the claim indefinite.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

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3. Resolving the level of ordinary skill in the pertinent art.
 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
8. Claims 1, 5-7, 21-22, 40, 279, 307, 341, 343, 345 and 347-356 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heinrichs et al. (WO 01/25438, 04/12/2001-cited by the Applicant) view of Jensen et al. (WO/01/36001, 05/25/2001-cited in the previous Office action) in further in view of Walter MR (Seminars in Oncology, 24, S9-52-S9-62, 1997), Bernkop-Schnürch (J. Controlled release, 52,1-16,1998), Blank et al. (Eur. J. Biochem., 265, 11-19, 1999-cited in the previous Office action), Sheppard P. (U.S. Pat. 6,153,420-cited in the previous Office action) Yan et al. (Biochemistry, 23, 3759-3765, 1984) and Black et al. (J. Biol. Chem. , 264, 5323-5326, 1989).

The claims are drawn to an isolated interferon (IFN) alpha cytokine, comprising an amino acid replacement in its sequence of amino acids, whereby the interferon alpha cytokine exhibits increased resistance to proteolysis compared to the unmodified interferon alpha cytokine that does not comprise the amino acid replacement; wherein an amino acid replacement is E41Q or the corresponding position, based upon alignment, in the interferon-alpha cytokine. Further limitations comprise specific members of interferon alpha subfamily and the number of mutations may be higher than two. Also claimed is a pharmaceutical composition comprising the mutant claimed. Specific mutations are claimed such as E41Q and D94G.

As presented in the previous Office action, Heinrichs et al teach novel interferon-alpha homologue polypeptides by teaching methods for identifying IFN- α homologues

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having altered properties or activities such as enhanced antiviral, antiproliferative, growth inhibitory, cytostatic, cytotoxic activity or reduced immunogenicity. Heinrichs et al. also teaches that the resulting polypeptides can be further modified, for example, to increase serum half-life, reduce antigenicity, or increase polypeptide stability and teaches that such modifications include glycosylation, sulfatation, PEGylation, phosphorylation, etc. The mutants of the invention posses clinical utility in that they are designed towards optimization for use as pharmaceuticals and to overcome dose-limiting toxicity, receptor cross-reactivity, and short serum half-lives significantly reduce the clinical utility of many of these cytokines. The existence of abundant naturally occurring sequence diversity within the interferon-alphas (and hence a large sequence space of recombinants) along with the intricacy of interferon-alpha/receptor interactions and variety of therapeutic and prophylactic activities creates an opportunity for the construction of superior interferon homologues (p. 2-3). Thus, Heinrichs et al. teaches a directed evolution method by which one could identify interferon mutants that have enhanced antiviral, antiproliferative, growth inhibitory, cytostatic, cytotoxic activity or reduced immunogenicity, or having other property such as low immunogenicity, increased half-life, improved solubility or oral availability. As such, Heinrichs present evidence of the feasibility of obtaining IFN compounds with better characteristics, the motivation to do it and some means of accomplishing the goals, for instance for greater oral availability. Also as mentioned, in the previous action, Heinrichs et al. do not specifically teach the mutation E41Q or D94G.

Jensen et al. teach interferon-gamma compounds that are modified by removing amino acid residues or introducing amino acid residues that can be further used for attaching a non-polypeptide moiety. The compounds have extended half-life in vivo and improved stability towards proteolysis (p. 4, lines 1-6). The compounds may also be IFN γ variants or fragments, wherein the variants differ in one or more amino acid residues from its parent polypeptide, normally in 1, 2, 3, 4, 5, 6, 7, 8, 9, 25 10, 11, 12, 13, 14 or 15 amino acid residues and fragments are a part of the full-length human IFN- γ , either C-terminally or N-terminally truncated (p.9 line 31 to p. 10, line 27). The compounds can be formulated in a pharmaceutical composition in a variety of forms, including liquid, gel, lyophilized, powder, compressed solid, or any other suitable forms, to be administered orally, separate or in conjunction with other therapeutic agents (p.38, lines 10-30). The compositions contain excipients (buffering agents, stabilizing agents, preservatives, isotonifiers, non-ionic detergents, antioxidants and/or other miscellaneous additives) (p40, line 14 to p.42, line 30). The compositions for oral administration are specifically taught (p. 42, line 33 to p. 43, line 29). Jensen et al. also teach the introduction of E38N glycosylation site in IFN γ , to obtain a protease resistant mutant for a position of the residues, which exposed at least 50% to the surface of the polypeptide (p. 16, line 32 to p.17, line 2). The most important teaching of Jensen is that the E38 of the IFN γ is at a surface exposed protein site, an exposed site that is a prerequisite for a proteolytic attack.

Walter MR teaches that the residues E41, D94 and R23 are exposed residues in the molecule of Interferon alpha (IFN α) (figure 4) and thus exposed to a proteolytic attack.

Bernkop-Schnürch teaches that a sufficient bioavailability of the therapeutic agents after oral dosing, several barriers encountered with the gastrointestinal (GI) tract have to be overcome. One of these barriers is caused by proteolytic enzymes, leading to a severe presystemic degradation in the GI tract (abstract).

Blank et al. teach possible cleavage sites for the IFN α -2b molecule (Fig. 5), which include the E41 residue, which is a cleavable site for Glu-C protease (as indicated by the boxed residues).

Sheppard teaches a novel serine protease homologous to glutamyl endopeptidases (Glu-C proteases) which are found in tissues exposed to the external environment, like small intestine and colon (col. 5, line 21 to col. 6, line 31), which would be the site of degradation of an orally administered composition.

Yan et al. teach introduction of glycosyl units at glutamines by transglutaminases and thus facilitate the internalization of the glycoproteins (Abstract and p. 3759, right col., lines 1-5 of the article).

Black et al. teach a pre-aspartate specific protease from the human leukocytes (abstract). The protease was identified in the conditioned medium from human peripheral blood mononuclear cells and is unique in its requirement of an aspartate as a recognition site since the enzyme is not active even if such mutations of the aspartate is made with very similar amino acids like glutamate or asparagine. (Discussion section).

It would have been obvious for a person of ordinary skill in the art at the time that the invention was made to combine the teachings of Heinrichs et al. with the teachings Jensen et al., Walter MR, Bernkop-Schnürch, Blank et al., Sheppard et al., Yan et al. and Black et al. to obtain IFN- α compounds and compositions containing surface exposed residues that are protected and thus conferring resistance to proteolysis with a reasonable expectation of success. This is because the exposed site are known and also proteases that are encountered at the site where the composition would be administered is uncovered by Sheppard et al. or at sites where the compounds would be present (like in the blood) is disclosed by Black et al. The motivation to do so would have been offered by the advantages of the compositions taught by Heinrichs et al. and Jensen et al with respect to the proteolytic resistance of the modified mutants. Also the teaching of Jensen et al., read in the light of Walter and Yan et al. would have made it obvious for a person of ordinary skill in the art to try a limited number of surface exposed positions in the IFN- α to be mutated to obtain better products. The E41 is just one of the limited residues that could be tried because, on one hand, by mutating it first eliminates a potential site for glutamyl endopeptidases (like the enzyme taught by Sheppard) which would degrade the IFN- α 2 and thus make it unusable for therapy. Such as enzyme, found in small intestine and colon, would severely impede the absorption of IFN- α 2 and increase the dosage necessary for therapy and thus could reach its toxicity limit. A person of ordinary skill in the art would have had a finite number of amino acids to choose from changing the E41. An additional motivation to choose the glutamine (Q) as a mutation for E41 is the finding of Yan et al. that

glutamine can be glycosylated and the glycosylated product might have an easier task of being internalized in the cell. Once the IFN- α has passed into the blood stream it might have encountered a protease as described by Black et al. and thus protection against it would become obvious by employing the teaching of Walter and mutate the D94 site. The choice for Glycine would assure a minimal surface exposure given the small size of this amino acid. Thus, a comprehensive reading of the references would necessarily lead a person of ordinary skill in the art to make the substitution E41Q and D94G since a skilled artisan has good reason to pursue known options in her or his technical grasp.

On page 33 of the Remarks Applicant argues that, in the reference, that in Jensen et al. it is the conjugates, not the polypeptides, which exhibit improved stability towards proteolysis, which is correct. Applicant argues that Jensen et al. also does not teach or suggest that its conjugates, by virtue of increased protease resistance can be administered orally and rendered orally available. This is factually incorrect since compositions for oral administration are specifically taught (p. 42, line 33 to p. 43, line 29).

Further, Applicant concludes that “Jensen et al. fails to teach virtually any of the elements of the instantly claimed compositions.”

The arguments were carefully considered but not found persuasive because the most important notion underscored by Jensen et al. and explained in the previous Office action is that the E38 of the IFN γ is at an protein surface exposed site and it is

desirable to protect the surface exposed sites that might be sensitive to proteolysis (or glycosylation for example in Jensen et al.'s case).

On page 34 of the Remarks Applicant argues that Sheppard et al. provides no[t] (sic) teachings or suggestions that are of any relevance to the instant claims.

The arguments were carefully considered but not found persuasive because as iterated in the previous Office action, Sheppard teaches a novel serine protease homologous to glutamyl endopeptidases (Glu-C proteases) which are found in tissues exposed to the external environment, like small intestine and colon (col. 5, line 21 to col. 6, line 31), which would be the site of degradation of an orally administered composition. The person of ordinary skill in the art does not have to have the same motivation as the Sheppard et al. to use the Glu-C protease as exactly taught by them. The rational trend of thought would be that, if this protease is encountered in the digestive tract, it would represent a set back for therapy procedures that are based on orally administered compounds which have exposed E residues. Thus, while administered to the gastro intestinal tract, the compound would be exposed to the attack of the Glu-C protease at a site taught by Blank et al.

On page 32 of the Remarks Applicant argues that Blank et al. does not teach a Glu41 cleavage site in IFN α .

The arguments were carefully considered but not found persuasive because Blank et al. teach possible cleavage sites for the IFN α -2b molecule (Fig. 5), which include the E41 residue, which, contrary to Applicants assertion in the remarks, is a cleavable site for Glu-C protease, as indicated by the boxed residues.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heinrichs et al. (WO 01/25438, 04/12/2001-cited by the Applicant) view of Jensen et al. (WO/01/36001, 05/25/2001) in further in view of Walter MR (Seminars in Oncology, 24, S9-52-S9-62, 1997, Bernkop-Schnürch (J. Controlled release, 52,1-16,1998), Blank et al. (Eur. J. Biochem., 265, 11-19, 1999), Sheppard P. (U.S. Pat. 6,153,420) Yan et al. (Biochemistry, 23, 3759-3765, 1984) and Pang DZD (U.S. Pat. No. 6,319,691).

The claim is drawn to an isolated modified interferon alpha cytokine comprising the sequence of amino acids set forth in any of SEQ ID NOS: 2-17, 19-131, 134-181, 978-988 and 1303 wherein the arginine at position 23 in each SEQ ID is replaced with a lysine.

The teachings of Heinrichs et al., Jensen et al. , Walter MR, Bernkop-Schnürch, Blank et al., Sheppard P. , Yan et al. were presented *supra*. They are silent about the R23K substitution.

Pang et al. teach fusion proteins which comprise human IFN-alpha and human TM-alpha1 (abstract). Further, the author teaches about three natural IFN-alpha 2 variants which have a substitution of a lysine for arginine at position 23 in the mature IFN-alpha2a protein and an arginine for histidine at position 34 in the mature IFN-alpha2c proteins. These differ significantly in their biologic and antigenic properties, indicating that differences in the amino acid sequences at position 23 and 34 may be significant in changing the immunogenicity as well as the structure and function of IFN-alpha2 (col. 1, lines 31-67).

It would have been obvious for person of ordinary skill in the art at the time that the invention was made to have adapted the teachings of Heinrichs et al., Jensen et al., Walter MR, Bernkop-Schnürch, Blank et al., Sheppard P., and Yan et al. for the IFN-alpha R23 mutants of Pang et al with a reasonable expectation of success. This is because the R23 variants were naturally occurring and the E41 Q mutation would have occurred to a naturally viable product. The motivation to do so stems from the fact that a skilled artisan has good reason to pursue known options in her or his technical grasp.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 5-7, 21-23, 40, 279, 307, 341, 343, 345 and 347-356 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 68-70, 72-74, 81-82, 84, 86, 89-90 of copending Application No. 11/176830. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to proteolytic resistant Interferon variants or compositions containing the same.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

10. No claims are allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ELLY-GERALD STOICA whose telephone number is (571)272-9941. The examiner can normally be reached on 8:30-17:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christine J Saoud/

Primary Examiner, Art Unit 1647